II. REMARKS

PRELIMINARY REMARKS

Claims 5, 7, and 24-26

Claims 5 and 7 have been rewritten in independent form in view of the examiner's indication of allowable subject matter.

Support for new claim 24 is found throughout the specification and claims as originally filed. Support for new claims 25 and 26 may be found at page 5, lines 10-14 of the specification as originally filed. No new matter is believed to have been introduced herein.

Information Disclosure Statements

At page 2 of the official action mailed May 6, 2002, the examiner indicated that the applicants' Information Disclosure Statements of May 21, 2002, and October 12, 2002 had been considered. In reviewing the official action, the applicants have noted that while an initialized copy of the applicants' Information Disclosure Statement dated May 21, 2002, was included in the mailing, an initialized copy of the applicants' Information Disclosure Statement dated October 12, 2002, was not enclosed. The applicants respectfully request that the examiner provide the initialized copy with the next communication from the Patent Office.

Objections to the Specification

The examiner objected to use of the language "gpm gene" at page 1, line 11 of the specification. The examiner also objected to use of the language "gpm: gpm gene from C. glutamicum" at page 17, line 24 of the specification. Alternate definitional language was suggested for both objections. In view of the foregoing amendment, the applicants submit that the objections are now moot. The applicants have further defined the gpm gene as a gene "which encodes phosphoglycerate mutase."

The examiner also objected to the abstract as originally filed. By the foregoing amendment the applicants have supplied a replacement abstract that is believed to comply with current Patent Office rules and procedures.

In view of the foregoing, the applicants request that the present objections to the specification and abstract be withdrawn.

Objections to the Claims

The examiner objected to claims 6, 22 and 23 as allegedly containing informalities. Specifically, the examiner objected to use of the language "replicatable," "Coryneform," and "Microorganism" in the claims, respectively. The applicants submit that these objections are now moot. The language "replicatable" has been removed from claim 6, while the language "Coryneform" in claim 22 has been replaced with "A member of the Coryneform group of bacteria..." Finally, the language "Microorganism" has been removed from claim 23.

The examiner also objected to claims 5 and 7 as depending from rejected claim 2. By the foregoing amendment, claims 5 and 7 have been rewritten in independent.

In view of the foregoing amendment and remarks, the applicants respectfully request that the objection to claims 5-7, 22, and 23 be withdrawn.

PATENTABILITY REMARKS

The Rejection of Claims 1-7 and 21-23 Under
35 U.S.C. §112, Second Paragraph Should be Withdrawn

The examiner rejected claims 1-7 and 21-23 under 35 U.S.C. §112, second paragraph, for allegedly containing indefinite language. The examiner's rejection refers to use of the terminology "hybridizes" Specifically, the examiner alleged that the term is unclear absent a statement of the conditions under which the hybridization reaction is performed.

The applicants respectfully traverse this rejection and submit that claims 1-5 and 21-23 have been improperly rejected in that these claims do not contain the terminology, "hybridizes" as alleged by the examiner. Claim 6 has been amended, for the purpose of expediting prosecution and without prejudice to the applicants' right to seek such a claim in a continuing application, by removing the terminology referred to by the examiner.

The applicants submit further that this specific rejection should not be extended to new claim 24. It is the applicants' position that claim 24 is not indefinite in that the claim d, through the use of functional language, defines a discrete group of polynucleotides that must encode a protein having the enzymatic activity of phosphoglycerate mutase.

Claims 2 and 6 were rejected for the alleged indefinite term "replicatable." The examiner stated that "[a]s any DNA is replicable (i.e. capable of replication) given its insertion in the proper vector and cell environment, it is unclear how this claim further limits

claim 1 from which it depends." The examiner also indicated that if it was the applicants' intent to claim a DNA expression vector, then the claim should be amended as such.

The applicants respectfully traverse this rejection and submit that they do not read the ability of the claimed DNA to replicate in corynebacterial cells to mean the claims are intended to be directed to an expression vector. Amended claims 2 and 6 reflect this understanding.

Claim 6 was further rejected as allegedly being indefinite for use of the language "neutral sense in (i)." The examiner alleged that the applicants must be referring to something other than a degenerate in part (iv) of the claim.

The applicants respectfully traverse this rejection of claim 6 and submit that as amended here, the claim is not indefinite. Specifically, the applicants have amended claim 6 to more clearly define the applicants' invention as set forth by the claims (introduction of a function maintained in the face of a neutral sense mutation).

Claim 22 was rejected as being indefinite for use of the language "Coryneform microorganisms." The examiner alleged that it is unclear what, in addition to microorganisms from the genus Corynebacterium, do applicants consider to be a Coryneform microorganism. Also, the examiner alleged that claim 23 does not further define claim 22, asserting that "Coryneform microorganisms means Corynebacterium. For similar reasons, the examiner alleged that claim 1 was indefinite.

The applicants respectfully traverse. The phrase "Coryneform microorganisms" as used in the specification refers to the Coryneform group of bacteria, which includes such rod-shaped microorganisms as members of the *Corynebacterium*, *Arthrobacter*, *Cellulomonas*, *Kurthia*, and *Brevibacterium* (See pages 6 and 7 of the specification; See also, Appendix B). The applicants believe that there may be a misunderstanding of the basic microbial taxonomy involved in practicing embodiments of the invention. To further clarify the metes and bounds of the applicants claimed invention, the applicants have amended claim 22 to be directed to "[a] member of the Coryneform group of bacteria transformed by the introduction of the polynucleotide according to one of claims 1 or 6." Claim 23 has been amended to recite "[b]acteria transformed according to claim 22, wherein the bacteria are of the genus Corynebacterium." Finally, claim 1 has been amended to recite "an isolated corynebacterial polynucleotide…"

In view of the foregoing amendment and remarks, the applicants submit that claims 1-7 and 21-23 are not indefinite and therefore request that the rejections based upon 35 U.S.C §112, second paragraph be withdrawn.

The Rejection of Claims 1-4, 6, and 21-23 Under 35 U.S.C. §112, First Paragraph Should be Withdrawn

The examiner rejected claims 1-4, 6, and 21-23 under 35 U.S.C. §112, first paragraph as allegedly containing subject matter not supported by a sufficient written description or an enabling specification. In particular, the examiner stated that the claims are unduly broad because they do not restrict the coverage to polynucleotides encoding polypeptides having the function of the polypeptide encoded by the polynucleotide defined by SEQ ID NO: 1.

The applicants respectfully traverse and submit that as amended herein, claims 1-4, 6, and 21-23 do not contain subject matter not supported by a sufficient written description nor are they broader than the enabling disclosure. Specifically, claims 1 and 6 have been amended to include the requirement that the variously claimed polynucleotides encode a polypeptide having phosphoglycerate mutase activity. Therefore, claims 1 and 6 are directed to a discrete and finite number of polynucleotides and neither lack written descriptive support nor are the claims broader than the enabling disclosure. Therefore, the applicants respectfully request that the rejection of claims 1-4, 6, and 21-23 under 35 U.S.C. §112, first paragraph be withdrawn.

The Rejection of Claims 1-4, 6, and 21 Under 35 U.S.C. §102(a) Should be Withdrawn

The examiner rejected claims 1-4, 6, and 21 under 35 U.S.C. §102(a) for allegedly being anticipated by White *et al.* (*J. Bacteriology*, 174(2):434-440, Jan. 1992). The examiner stated that the polynucleotide taught by White *et al.* has a best local similarity score of 68.7% relative to SEQ ID NO: 1, including many regions of higher sequence identity comprising at least 15 contiguous bases of SEQ ID NO: 1. The examiner stated further that while the sequences taught by the cited document were not isolated from corynebacteria, as discussed

in the section directed to rejections based upon 35 U.S.C. §112, second paragraph, the examiner is of the believe that this is not a necessary limitation to the claims.

The applicants respectfully traverse and submit that claims 1-4, 6, and 21 are novel over the disclosure of White *et al.* For a prior art reference to anticipate in terms of 35 U.S.C. §102 every element of the claimed invention must be identically shown in a single reference. In re Bond 15 USPQ2d 1566, 1567 (Fed. Cir. 1990). The examiner simply has not established a *prima facie* case of anticipation in that the cited document does not disclose isolated polynucleotides from corynebacteria. In other words, claims requiring an isolated polynucleotide from corynebacteria cannot be anticipated by a polynucleotide isolated from *Streptomyces coelicolor*. Further, a similarity score of 68.7 is simply not at least 70% identical to a polynucleotide encoding a polypeptide containing the amino acid sequence of SEQ ID 2, as required by the present claims.

With respect to the examiner's comment that the term "corynebacteria" is believed not to be necessary, the applicants submit that the examiner's position is misplaced. As discussed above with respect to 35 U.S.C. §112, second paragraph, the terminology is important for defining the metes and bounds of the applicants' claimed invention. As such (and as also discussed above), the applicants have, in view of what is thought to be a misunderstanding of basic microbial taxonomy, amended the claims to more clearly define the subject matter of their claimed invention.

In view of the foregoing amendment and remarks, the applicants submit that While *et al.* does not properly anticipate the applicants' claimed invention and therefore the examiner has failed to find a *prima facie* case of anticipation. Therefore, the applicants respectfully request that the rejection of claims 1-4, 6, and 21 under 35 U.S.C. §102(a) over White *et al.* be withdrawn.

III. CONCLUSION

In view of the foregoing, the claims are now believed to be in form for allowance, and such action is hereby solicited. If any point remains in issue that the examiner feels may be best resolved through a personal or telephone interview, the examiner is urged to contact the undersigned at the telephone number indicated below.

Respectfully submitted,

Pillsbury Winthrop LLP

By: _____

Thomas A Cawley, Jr., Ph.D.
Reg. No.: 40,944
Tel. No.: (703) 905-2144
Fax No.: (703) 905-2500

TAC/
1600 Tysons Boulevard
McLean, VA 22102

(703) 905-2000
Enclosure: Appendix

APPENDIX A

VERSION WITH MARKINGS TO SHOW CHANGES MADE

SPECIFICATION

The paragraph at page 1, lines 10-13 of the specification was amended as follows.

The invention provides nucleotide sequences encoding the gpm gene, which encodes phosphoglycerate mutase, and fermentation processes for the preparation of amino acids, especially L-lysine, using corynebacteria in which the gpm gene is amplified.

The Brief Description of the Drawing of Figure 2 bridging pages 17 and 18 of the specification was amended as follows.

Figure 2: Map of plasmid PxKgpmexp

The abbreviations and symbols are defined as follows:

per: copy of number control gene from pGA1

oriE: plasmid-coded origin of replication from E. coli

rep: plasmid-coded origin of replication from C. glutamicum plasmid pGA1

Ptrc: trc promoter from pTRC99A

T1, T2: terminator regions 1 and 2 from pTRC99A

lacIq: repressor gene of the lac operon

Kan: kanamycin resistance gene

gpm: gpm gene from C. glutamicum, which encodes phosphoglycerate mutase

EcoRI: cleavage site of the restriction enzyme EcoRI

Ecl136II cleavage site of the restriction enzyme ecl136II

HindIII cleavage site of the restriction enzyme HindIII

KpnI: cleavage site of the restriction enzyme KpnI

SalI: cleavage site of the restriction enzyme SalI

SmaI: cleavage site of the restriction enzyme SmaI

PstI: cleavage site of the restriction enzyme PstI

BamHI: cleavage site of the restriction enzyme BamHI

NcoI: cleavage site of the restriction enzyme NcoI

XbaI: cleavage site of the restriction enzyme Xba1

XmaI: cleavage site of the restriction enzyme XmaI

SacI: cleavage site of the restriction enzyme SacI

CLAIMS

Claims 1, 2, 5-7, 22, and 23 were amended as follows.

1. (Amended) An isolated corynebacterial polynucleotide [from corynebacteria which contains] comprising a polynucleotide sequence selected from the group consisting of:

a) a polynucleotide [which] that is at least 70% identical to a polynucleotide encoding a polypeptide containing the amino acid sequence of SEQ ID NO : 2, the polypeptide having phosphoglycerate mutase activity,

b) a polynucleotide encoding a polypeptide containing an amino acid sequence which is at least 70% identical to the amino acid sequence of SEQ ID NO : 2, the polypeptide having phosphoglycerate mutase activity,

c) a polynucleotide [which] that is complementary to the polynucleotides of a), or b), and

d) a polynucleotide containing at least 15 consecutive bases of the polynucleotide sequence of a), b) or c), the polynucleotide encoding a polypeptide having phosphoglycerate mutase activity.

2. (Amended) The polynucleotide according to Claim 1 which is a DNA [replicatable] that replicates in corynebacterial host cells [in corynebacteria].

5. (Amended) An isolated corynebacterial polynucleotide comprising a polynucleotide sequence selected from the group consisting of:

a) a polynucleotide that is at least 70% identical to a polynucleotide encoding a polypeptide containing the amino acid sequence of SEQ ID NO : 2, the polypeptide having phosphoglycerate mutase activity,

b) a polynucleotide encoding a polypeptide containing an amino acid sequence which is at least 70% identical to the amino acid sequence of SEQ ID NO : 2, the polypeptide having phosphoglycerate mutase activity,

c) a polynucleotide that is complementary to the polynucleotides of a), or b), and

d) a polynucleotide containing at least 15 consecutive bases of the polynucleotide sequence of a), b) or c), the polynucleotide encoding a polypeptide having phosphoglycerate mutase activity;

wherein the [The] polynucleotide [according to Claim 2 containing] comprises the nucleic acid sequence as shown in SEQ ID NO : 1 and replicates in corynebacterial host cells.

6. (Amended) The polynucleotide that is [Replicatble] DNA according to Claim 2 [containing] comprising:

(i) the nucleotide sequence shown in SEQ ID NO: 1, or

(ii) at least one sequence that is a degenerate variant of [corresponding to] sequence (i) within the degeneracy of the genetic code], or

(iii) the nucleotide sequence shown in SEQ ID NO: 1 in which a sense mutation has been introduced, wherein the mutated nucleotide sequence encodes for a polypeptide having phosphoglycerate mutase activity [at least one sequence which hybridizes with the sequence complementary to sequence (i) or (ii), and optionally

(iv) neutral sense mutation in (i)].

7. (Amended) An isolated corynebacterial polynucleotide comprising a polynucleotide sequence selected from the group consisting of:

a) a polynucleotide that is at least 70% identical to a polynucleotide encoding a polypeptide containing the amino acid sequence of SEQ ID NO : 2, the polypeptide having phosphoglycerate mutase activity,

b) a polynucleotide encoding a polypeptide containing an amino acid sequence which is at least 70% identical to the amino acid sequence of SEQ ID NO : 2, the polypeptide having phosphoglycerate mutase activity,

c) a polynucleotide that is complementary to the polynucleotides of a), or b), and

d) a polynucleotide containing at least 15 consecutive bases of the polynucleotide sequence of a), b) or c), the polynucleotide encoding a polypeptide having phosphoglycerate mutase activity;

wherein the [The] the polynucleotide [according to Claim 2 encoding] replicates in corynebacterial host cells and encodes a polypeptide [containing] comprising the amino acid sequence [as] shown in SEQ ID NO : 2.

22. (Amended) A member of the Coryneform group of bacteria [microorganisms] transformed by the introduction of the [replicatable DNA] polynucleotide according to one of Claims 1 or 6.

23. (Amended) Bacteria transformed [Microorganisms] according to claim 22, wherein the bacteria are of [from] the genus Corynebacterium.

New claims 24-26 were introduced by the foregoing amendment.

24. An isolated polynucleotide isolated from the species Corynebacterium glutamicum that hybridizes to the complement of SEQ ID NO: 1, wherein the isolated polynucleotide encodes a polypeptide having the enzymatic activity of phosphoglycerate mutase.

25. An isolated polynucleotide comprising at least 30 consecutive nucleotides of SEQ ID NO: 1 having the function of a primer in a polymerase chain reaction to produce a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO: 2.

26. An isolated polynucleotide comprising at least 30 consecutive nucleotides of the complement to SEQ ID NO: 1 having the function of a probe in a hybridization reaction to detect or to isolate a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO: 2.